



PTO/SB/21 (09-04)

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**TRANSMITTAL
FORM**

(to be used for all correspondence after initial filing)

Total Number of Pages in This Submission

Application Number	10/724,833
Filing Date	December 2, 2003
First Named Inventor	Thomas Nelson
Art Unit	1653
Examiner Name	Rooke, Agnes Beata
Attorney Docket Number	17357.01302US

ENCLOSURES (Check all that apply)

- | | | |
|---|---|---|
| <input checked="" type="checkbox"/> Fee Transmittal Form | <input type="checkbox"/> Drawing(s) | <input type="checkbox"/> After Allowance Communication to TC |
| <input checked="" type="checkbox"/> Fee Attached | <input type="checkbox"/> Licensing-related Papers | <input type="checkbox"/> Appeal Communication to Board of Appeals and Interferences |
| <input type="checkbox"/> Amendment/Reply | <input type="checkbox"/> Petition | <input type="checkbox"/> Appeal Communication to TC (Appeal Notice, Brief, Reply Brief) |
| <input type="checkbox"/> After Final | <input type="checkbox"/> Petition to Convert to a Provisional Application | <input type="checkbox"/> Proprietary Information |
| <input type="checkbox"/> Affidavits/declaration(s) | <input type="checkbox"/> Power of Attorney, Revocation | <input type="checkbox"/> Status Letter |
| <input type="checkbox"/> Extension of Time Request | <input type="checkbox"/> Change of Correspondence Address | <input checked="" type="checkbox"/> Other Enclosure(s) (please identify below): |
| <input type="checkbox"/> Express Abandonment Request | <input type="checkbox"/> Terminal Disclaimer | |
| <input checked="" type="checkbox"/> Information Disclosure Statement | <input type="checkbox"/> Request for Refund | |
| <input type="checkbox"/> Certified Copy of Priority Document(s) | <input type="checkbox"/> CD, Number of CD(s) _____ | |
| <input type="checkbox"/> Reply to Missing Parts/Incomplete Application | <input type="checkbox"/> Landscape Table on CD | |
| <input type="checkbox"/> Reply to Missing Parts under 37 CFR 1.52 or 1.53 | | |

Remarks

1. Copies of 21 References
2. Check 3827 (\$180.00)

SIGNATURE OF APPLICANT, ATTORNEY, OR AGENT

Firm Name	Milbank, Tweed, Hadley & McCloy LLP		
Signature			
Printed name	Einar Stole		
Date	December 15, 2004	Reg. No.	47,272

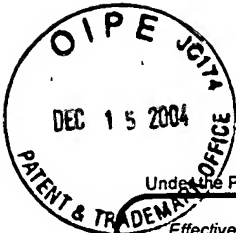
CERTIFICATE OF TRANSMISSION/MAILING

I hereby certify that this correspondence is being facsimile transmitted to the USPTO or deposited with the United States Postal Service with sufficient postage as first class mail in an envelope addressed to: Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450 on the date shown below:

Signature			
Typed or printed name		Date	

This collection of information is required by 37 CFR 1.5. The information is required to obtain or retain a benefit by the public which is to file (and by the USPTO to process) an application. Confidentiality is governed by 35 U.S.C. 122 and 37 CFR 1.11 and 1.14. This collection is estimated to 2 hours to complete, including gathering, preparing, and submitting the completed application form to the USPTO. Time will vary depending upon the individual case. Any comments on the amount of time you require to complete this form and/or suggestions for reducing this burden, should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, U.S. Department of Commerce, P.O. Box 1450, Alexandria, VA 22313-1450. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. SEND TO: Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450.

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PTO/SB/17 (11-04)

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Effective on 10/01/2004. Patent fees are subject to annual revision.

FEE TRANSMITTAL For FY 2005

☒ Applicant claims small entity status. See 37 CFR 1.27

TOTAL AMOUNT OF PAYMENT (\$) 180.00

Complete if Known

Application Number	10/724,833
Filing Date	December 2, 2003
First Named Inventor	Thomas Nelson
Examiner Name	Rooke, Agnes Beata
Art Unit	1653
Attorney Docket No.	17357.01302US

METHOD OF PAYMENT (check all that apply)☒ Check ☐ Credit Card ☐ Money Order☒ Deposit Account ☐ None

Deposit Account Number 13-3250

Deposit Account Name

The Director is hereby authorized to: (check all that apply)

☒ Charge fee(s) indicated below☐ Charge fee(s) indicated below, except for the filing fee☒ Charge any additional fee(s) or underpayments of fee(s) under 37 CFR 1.16 and 1.17☐ Credit any overpayments

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☐ Other (please identify):**WARNING:** Information on this form may become public. Credit card information should not be included on this form. Provide credit card information and authorization on PTO-2038.**FEE CALCULATION****1. BASIC FILING FEE**

Fee Description	Fee (\$)	Small Entity Fee (\$)	Fee Paid(\$)
Utility Filing Fee	790	395	
Design Filing Fee	350	175	
Plant Filing Fee	550	275	
Reissue Filing Fee	790	395	
Provisional Filing Fee	160	80	

Subtotal (1) \$

FEE CALCULATION (continued)**2. EXTRA CLAIM FEES**

Fee Description	Fee (\$)	Small Entity Fee (\$)
Each claim over 20	18	9
Each independent claim over 3	88	44
Multiple dependent claims	300	150
For Reissues, each claim over 20 and more than in the original patent	18	9
For Reissues, each independent claim more than in the original patent	88	44

Total Claims **Extra Claims** **Fee (\$)** **Fee Paid (\$)**- 20 or HP = $\frac{\text{Total Claims} - 20}{\text{Extra Claims}}$ x $\frac{\text{Fee ($)}}{\text{Fee Paid ($)}}$ =
HP = highest number of total claims paid for, if greater than 20**Indep. Claims** **Extra Claims** **Fee (\$)** **Fee Paid (\$)**- 3 or HP = $\frac{\text{Indep. Claims} - 3}{\text{Extra Claims}}$ x $\frac{\text{Fee ($)}}{\text{Fee Paid ($)}}$ =
HP = highest number of independent claims paid for, if greater than 3**Multiple Dependent Claims** **Fee (\$)** **Fee Paid (\$)**

Subtotal (2) \$

3. OTHER FEES

Fee Description	Fee (\$)	Small Entity Fee (\$)	Fee Paid(\$)
1-month extension of time	110	55	
2-month extension of time	430	215	
3-month extension of time	980	490	
4-month extension of time	1,530	765	
5-month extension of time	2,080	1,040	
Information disclosure stmt. fee	180	180	180.00
37 CFR 1.17(q) processing fee	50	50	
Non-English specification	130	130	
Notice of Appeal	340	170	
Filing a brief in support of appeal	340	170	
Request for oral hearing	300	150	
Other:			

Subtotal (3) \$ 180.00

SUBMITTED BY

Signature

Einar Stole

Registration No.

(Attorney/Agent) 47,272

Telephone

202-835-7553

Name (Print/Type)

Date December 15, 2004

This collection of information is required by 37 CFR 1.136. The information is required to obtain or retain a benefit by the public which is to file (and by the USPTO to process) an application. Confidentiality is governed by 35 U.S.C. 122 and 37 CFR 1.14. This collection is estimated to take 30 minutes to complete, including gathering, preparing, and submitting the completed application form to the USPTO. Time will vary depending upon the individual case. Any comments on the amount of time you require to complete this form and/or suggestions for reducing this burden, should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, U.S. Department of Commerce, P.O. Box 1450, Alexandria, VA 22313-1450. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. SEND TO: Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450.

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ATTORNEY DOCKET NO. 17357.01302US

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Application of:)
Thomas Nelson) Group Art Unit: 1653
Filed: December 2, 2003) Examiner: Rooke, Agnes Beata
For: *Artificial Low-Density Lipoprotein*)
Carriers for Transport of Substances)
Across the Blood-Brain Barrier)

INFORMATION DISCLOSURE STATEMENT

Mail Stop DD

Commissioner of Patents
U.S. Patent and Trademark Office
P.O. Box 1450
Alexandria, VA 22313-1450

Sir:

In accordance with 37 C.F.R. §§ 1.97 and 1.98, and in compliance with the duty of disclosure set forth in C.F.R. § 1.56, applicants are submitting herewith copies of references listed on the attached Forms PTO/SB/08A and PTO/SB/08B for consideration and to be made of record herein by the U.S. Patent and Trademark Office in the above-captioned application.

Consideration of the foregoing plus the prompt return of a copy of the enclosed Forms PTO/SB/08A and PTO/SB/08B with the Examiner's initials in the left column in accordance with MPEP 609 are respectfully requested.

Applicants' submission of the Information Disclosure Statement (IDS) shall not be construed as an admission that the cited references are prior art to the present invention, or that the cited references qualify as printed publications. The submission of this IDS also shall not be construed as a representation that a prior art search has been performed.

In accordance with 37 C.F.R. § 1.97(c), this Information Disclosure Statement is believed submitted before the mailing of a final Official Action and is accompanied by the required fee under § 1.17(p). In the even any additional fee is deemed necessary, the Commissioner is authorized to charge the undersigned's Deposit Account No. 13-3250 under referenced No. 17357.01302US.

12/16/2004 ZJUXAR1 00000022 10724833

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180.00 CP

DC1:#8110109

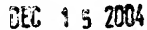
Respectfully submitted,

MILBANK, TWEED, HADLEY & McCLOY LLP

December 15, 2004

By: 
Einar Stole
Registration No., 47,272

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Complete if Known

(Use as many sheets as necessary)

Sheet 1 of 4

Application Number	10/724,833
Filing Date	December 2, 2003
First Named Inventor	Thomas Nelson
Art Unit	1653
Examiner Name	Rooke, Agnes Beata
Attorney Docket Number	17357.01302US

[illegible]

FOREIGN PATENT DOCUMENTS						
Examiner Initials*	Cite No. ¹	Foreign Patent Document	Publication Date	Name of Patentee or Applicant of Cited Document	Pages, Columns, Lines, Where Relevant Passages Or Relevant Figures Appear	T ⁶
		Country Code ³ Number ⁴ Kind Code ⁵ (if known)	MM-DD-YYYY			
		WO 98/13385	04/02/1998	Univ. of Strathclyde		
		WO 99/04761	02/04/1999	Pharmacia & Upjohn		
		EP 0 277 849 A1	08/10/1988	Ire Celltag SA		
		WO WO 92/21330	12/10/1992	Samain et al.		
		WO 87/02061	04/09/1987	Protter et al.		

Date	
Considered	

This collection of information is required by 37 CFR 1.97 and 1.98. The information is required to obtain or retain a benefit by the public which is to file (and by the USPTO to process) an application. Confidentiality is governed by 35 U.S.C. 122 and 37 CFR 1.14. This collection is estimated to take 2 hours to complete, including gathering, preparing, and submitting the completed application form to the USPTO. Time will vary depending upon the individual case. Any comments on the amount of time you require to complete this form and/or suggestions for reducing this burden, should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, P.O. Box 1450, Alexandria, VA 22313-1450. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. SEND TO: Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450.

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Substitute for form 1449/PTO INFORMATION DISCLOSURE STATEMENT BY APPLICANT (Use as many sheets as necessary)		Complete if Known	
		Application Number	10/724,833
		Filing Date	December 2, 2003
		First Named Inventor	Thomas Nelson
		Art Unit	1653
		Examiner Name	Rooke, Agnes Beata
Sheet 2	of 4	Attorney Docket Number	17357.01302US

NON PATENT LITERATURE DOCUMENTS			
Examiner Initials*	Cite No. ¹	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.), date, page(s), volume-issue number(s), publisher, city and/or country where published.	T ²
		Rensen et al., "Human Recombinant Apolipoprotein E-Enriched Liposomes Can Mimic Low-Density Lipoproteins as Carriers for the Site-Specific Delivery of Antitumor Agents." Molecular Pharmacology, 52:445-455, September 1997, XP-002273272	
		Kreuter et al., "Apolipoprotein-mediated Transport of Nanoparticle-bound Drugs Across the Blood-Brain Barrier." Journal of Drug Targeting, 2002 Vol. 10(4) pp. 317-325, XP009027368	
		Versluis et al., "Synthesis of a Lipophilic Daunorubicin Derivative and Its Incorporation into Lipidic Carriers Developed for LDL Receptor-Mediated Tumor Therapy." Pharmaceutical Research, Vol. 15, No. 4, 1998, XP009036781	
		Masquelier et al., "Low Density Lipoprotein as a Carrier of Cytostatics in Cancer Chemotherapy: Study of Stability of Drug-Carrier Complexes in Blood." Journal of Drug Targeting, 2000, Vol. 8, No. 3, pp. 155-164, XP009027575	
		Masquelier et al., "Plasma stability and cytotoxicity of lipophilic daunorubicin derivatives incorporated into low density lipoproteins." Eur. J. Med. Chem. 35 (2000) 429-438	
		Murtha et al., "Synthesis of the Cholesteryl Ester Prodrugs Cholesteryl Ibuprofen and Cholesteryl Flufenamate and Their Formulation into Phospholipid Microemulsions." 1088 Journal of Pharmaceutical Sciences, 83 (1994) September, No. 9, DC, US, XP 00465804	
		Rensen et al., "Recombinant lipoproteins: lipoprotein-like lipid particles for drug targeting." Advanced Drug Delivery Reviews 47 (2001) 251-276, XP-002273271	
		Bhattacharya et al., "Novel distamycin analogues: facile synthesis of cholesterol conjugates of distamycin-like oligopeptides." Tetrahedron Letters 42 (2001) 3499-3502, XP-002299552	
		Reinhardt, R.R. et al., "Insulin-Like Growth Factors Cross the Blood-Brain Barrier," Endocrinology, Vol. 135, No. 5	
		Witt, Ken A. et al., "Insulin Enhancement of Opioid Peptide Transport across the Blood-Brain Barrier and Assessment of Analgesic Effect," The Journal of Pharmacology and Experimental Therapeutics, Vol. 295, No. 3, 3100/866639	

Examiner Signature	Date Considered
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*EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

1 Applicant's unique citation designation number (optional). 2 Applicant is to place a check mark here if English language Translation is attached. This collection of information is required by 37 CFR 1.98. The information is required to obtain or retain a benefit by the public which is to file (and by the USPTO to process) an application. Confidentiality is governed by 35 U.S.C. 122 and 37 CFR 1.14. This collection is estimated to take 2 hours to complete, including gathering, preparing, and submitting the completed application form to the USPTO. Time will vary depending upon the individual case. Any comments on the amount of time you require to complete this form and/or suggestions for reducing this burden, should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, P.O. Box 1450, Alexandria, VA 22313-1450. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. SEND TO: Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450.

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		Application Number	10/724,833
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		First Named Inventor	Thomas Nelson
		Art Unit	1653
		Examiner Name	Rooke, Agnes Beata
Sheet 3	of 4	Attorney Docket Number	17357.01302US

NON PATENT LITERATURE DOCUMENTS			
Examiner Initials*	Cite No. ¹	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.), date, page(s), volume-issue number(s), publisher, city and/or country where published.	T ²
		Rigotti, Attilio et al., "The Class B Scavenger Receptors SR-BI and CD36 Are Receptors for Antonic Phospholipids," The Journal of Biological Chemistry, Vol. 270, No. 27, Issue of July 7, pp. 16221-16224, 1995	
		Bradley, William et al., "Low-density Lipoprotein Receptor Binding Determinants Switch from Apolipoprotein E to Apolipoprotein B during Conversion of Hypertriglyceridemic Very-low-density Lipoprotein to Low-density Lipoproteins." The Journal of Biological Chemistry, Vol. 259, No. 23, Issue of December 10, pp. 14728-14735, 1984	
		Veingergs, Isaac et al., "Neurotoxic Effects of Apolipoprotein E4 are Mediated via Dysregulation of Calcium Homeostasis," Journal of Neuroscience Research 67:379-387 (2002)	
		Shibata, Masayoshi et al., "Clearance of Alzheimer's amyloid-B1-40 peptide from brain by LDL receptor-related protein-1 at the blood-brain barrier," The Journal of Clinical Investigation, December 2000, Vol. 106, No. 12	
		Alyaudtin, Renad et al. "Interaction of Poly(butylcyanoacrylate) Nanoparticles with Blood-Brain Barrier in vivo and in vitro," Journal of Drug Targeting, 2001, Vol. 9, No. 3, pp. 209-221	
		Kang, Young-Sook et al., "Stability of the Disulfide Bond in an Avidin-Biotin Linked Chimeric Peptide During in vivo Transcytosis Through Brain Endothelial Cells," Journal of Drug Targeting, 2000, Vol. 8, No. 6, pp. 425-434	
		Pardridge, William M., "CNS Drug Design Based on Principles of Blood-Brain Barrier Transport," J. Neurochem., Vol. 70, No. 5, 1998	
		Bickel, Ulrich et al., "Delivery of peptides and proteins through the blood-brain barrier," Advanced Drug Delivery Reviews, 10 (1993) 205-245	
		Hevonoja, Tiia et al., "Structure of low density lipoprotein (LDL) particles: Basis for understanding molecular changes in modified LDL," Biochemica et Biophysica Acta 1488 (2000) 189-210	
		Pardridge, William M. et al., "Blood-Brain Barrier: Interface Between Internal Medicine and the Brain," Annals of Internal Medicine, 1986; 105: 82-95	

Examiner Signature	Date Considered
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Sheet 4	of 4	Attorney Docket Number	17357.01302US

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		Wu, Dafang et al., "Pharmacokinetics and Brain Uptake of Biotinylated Basic Fibroblast Growth Factor Conjugated to a Blood-Brain Barrier Drug Delivery System," Journal of Drug Targeting, 2002 Vol. 10(3), pp. 239-245	
		Mims, Marth P. et al., "Effect of Particle Size and Temperature on the Conformation and Physiological Behavior of Apolipoprotein E Bound to Model Lipoprotein Particles," Biochemistry 1990, 29, 6639-6647	
		Holtzman, David M., "Role of apoE/AB Interactions in the Pathogenesis of Alzheimer's Disease and Cerebral Amyloid Angiopathy," Journal of Molecular Neurosciences, Vol. 17, 2001, pp. 147-155	

Examiner Signature		Date Considered	
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¹ Applicant's unique citation designation number (optional). ² Applicant is to place a check mark here if English language Translation is attached. This collection of information is required by 37 CFR 1.98. The information is required to obtain or retain a benefit by the public which is to file (and by the USPTO to process) an application. Confidentiality is governed by 35 U.S.C. 122 and 37 CFR 1.14. This collection is estimated to take 2 hours to complete, including gathering, preparing, and submitting the completed application form to the USPTO. Time will vary depending upon the individual case. Any comments on the amount of time you require to complete this form and/or suggestions for reducing this burden, should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, P.O. Box 1450, Alexandria, VA 22313-1450. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. SEND TO: Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450.

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